



# *MI FluFocus*

## **Influenza Surveillance and Avian Influenza Update**

**Bureau of Epidemiology  
Bureau of Laboratories**



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### ***New updates in this issue:***

- **Michigan:** Three specimens were positive for 2009 H1N1 influenza at MDCH BOL last week.
  - **National:** Research demonstrates that the 1918 and 2009 pandemic influenza viruses share a structural detail that makes both susceptible to neutralization by the same antibodies.
  - **International:** Vitamin D supplements may help prevent seasonal influenza and asthma attacks.
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### ***\*\*\*2009 Influenza A (H1N1) virus Updates\*\*\****

Please continue to reference the MDCH influenza website at [www.michigan.gov/flu](http://www.michigan.gov/flu) for additional 2009 H1N1 information. Local health departments can find guidance documents in the MI-HAN document library. In addition, additional laboratory-specific information is located at the Bureau of Laboratories H1N1 page at [http://www.michigan.gov/mdch/0,1607,7-132-2945\\_5103-213906--,00.html](http://www.michigan.gov/mdch/0,1607,7-132-2945_5103-213906--,00.html).

### ***\*\*\*Influenza Surveillance Reports\*\*\****

**Michigan Disease Surveillance System:** For the week ending March 20<sup>th</sup>, aggregate influenza, individual influenza, and 2009 novel influenza case levels were similar to the previous week's levels. All categories were lower than the levels seen at this time last year.

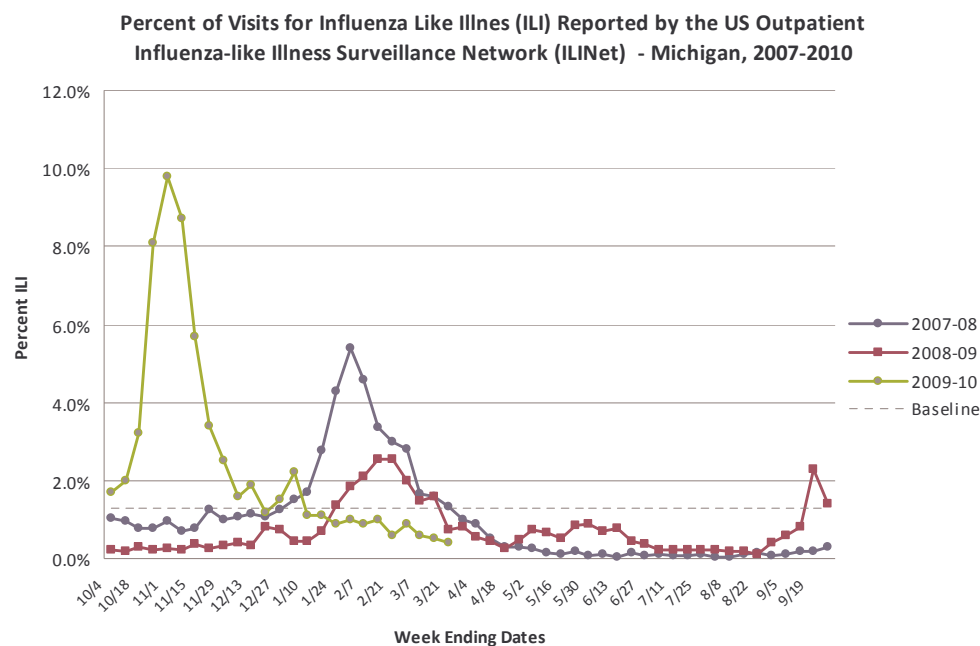
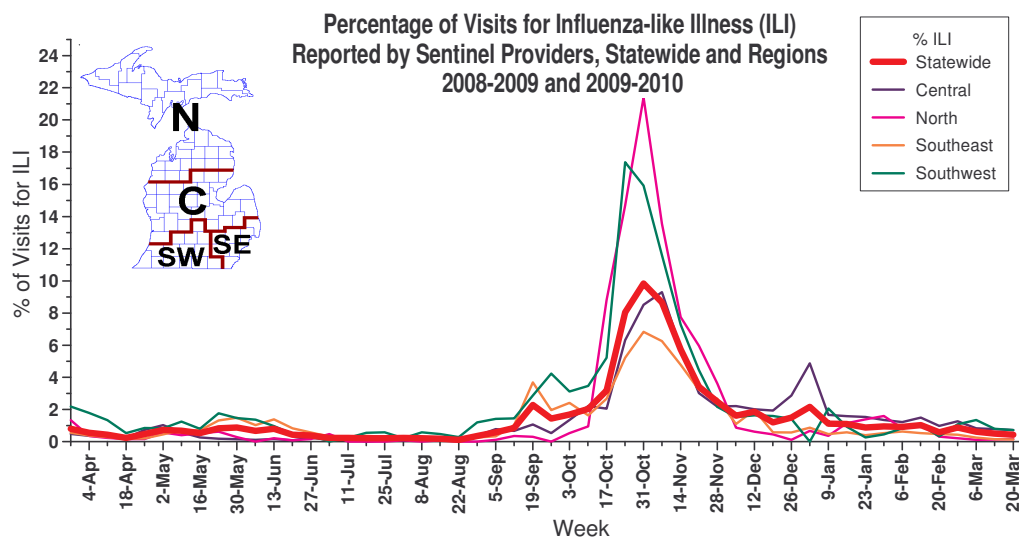
During March 14-20, 2010, 7006 cases of flu-like illness and confirmed and probable cases of seasonal and novel influenza were reported in Michigan. 2124 hospitalizations and 78 deaths associated with influenza have been reported since September 1, 2009. This report is updated every Tuesday by 5:00 pm and is accessible at "Current H1N1 Activity" on the website <http://www.michigan.gov/h1n1flu>.

**Emergency Department Surveillance:** Emergency department visits from constitutional and respiratory complaints were consistent with the previous week's levels. Constitutional and respiratory complaints are comparable to what was seen during this time last year. During the past week, there were three constitutional alerts in the N(2) and SW(1) Influenza Surveillance Regions and seven respiratory alerts in the C(5) and SE(2) Influenza Surveillance Regions.

**Over-the-Counter Product Surveillance:** Overall, OTC product sales were mostly steady over the last week. Pediatric electrolyte and thermometer sales increased slightly at the beginning of the week but returned to the previous week's levels by the end of the week. All indicators' sales were consistent with levels seen this time last year.

**Sentinel Provider Surveillance (as of March 25):** During the week ending March 20, 2010, the proportion of visits due to influenza-like illness (ILI) slightly decreased to 0.4% overall; 46 patient visits due to ILI were reported out of 10,683 office visits. Thirty sentinel sites provided data for this report. Activity slightly increased in one surveillance region: North (0.2%) and decreased in the remaining three surveillance regions: Southwest (0.7%), Central (0.7%) and Southeast (0.1%). Please note that these rates may change as additional reports are received.

As part of pandemic influenza surveillance, CDC and MDCH highly encourage year-round participation from all sentinel providers. New practices are encouraged to join the sentinel surveillance program today! Contact Cristi Carlton at 517-335-9104 or [CarltonC2@michigan.gov](mailto:CarltonC2@michigan.gov) for more information.



**Laboratory Surveillance (as of March 20):** During March 14-20, MDCH Bureau of Laboratories identified three 2009 H1N1 influenza A isolates. For the 2009-2010 season (starting on October 4, 2009), MDCH BOL has identified 609 influenza isolates:

- 2009 Influenza A (H1N1): 608
- Influenza B: 1

Nine sentinel labs reported for the week ending March 20, 2010. 2 labs reported sporadic influenza A activity (SE, C); all others reported zero influenza A positives (SE, SW, C, N). No labs reported influenza B positives. 7 labs reported sporadic or low levels of RSV positives (SE, SW, C, N), and 2 labs reported moderately elevated but decreasing RSV positives (SE, C).

**Michigan Influenza Antigenic Characterization (as of March 25):** One 2009 H1N1 influenza A virus from Michigan has undergone further characterization at the CDC. This virus was characterized as A/California/07/2009 (H1N1)-like, which is the recommended strain for the H1 component of the 2010-11 Northern Hemisphere vaccine.

**Michigan Influenza Antiviral Resistance Data (as of March 25):** Results are currently not available for antiviral resistance at CDC for the 2009-2010 season.

Antiviral resistance testing takes months to complete and cannot be used to guide individual patient treatment. However, CDC has made recommendations regarding the use of antivirals for treatment and prophylaxis of influenza. The guidance is available at <http://www.cdc.gov/H1N1flu/recommendations.htm>.

**Influenza-Associated Pediatric Mortality (as of March 25):** Five 2009 H1N1 influenza-associated pediatric mortalities (SE(3), SW, N) have been reported to MDCH for the 2009-2010 influenza season.

\*\*\*CDC has asked states for information on any pediatric death associated with influenza. This includes not only any pediatric death (<18 years) resulting from a compatible illness with laboratory confirmation of influenza, but also any unexplained pediatric death with evidence of an infectious process. Please immediately call MDCH to ensure proper specimens are obtained. View the complete MDCH protocol online at [http://www.michigan.gov/documents/mdch/ME\\_pediatric\\_influenza\\_guidance\\_v2\\_214270\\_7.pdf](http://www.michigan.gov/documents/mdch/ME_pediatric_influenza_guidance_v2_214270_7.pdf).

**Influenza Congregate Settings Outbreaks (as of March 25):** Seven congregate setting outbreaks with confirmatory novel influenza A H1N1 testing (2SE, 3 SW, 1C, 1N), and two outbreaks associated with positive influenza A tests (1C, 1N) have been reported to MDCH for the 2009-2010 influenza season. These are 8 school facilities and 1 long term care facility. Human metapneumovirus was confirmed in one outbreak in a long term care facility (SW) in February.

During fall 2009, 567 influenza-related school and/or district closures in Michigan (Public Health Preparedness Region 1 - 55, Region 2N - 4, Region 2S - 8, Region 3 - 54, Region 5 - 153, Region 6 - 100, Region 7 - 109, Region 8 - 84) were reported.

**National (CDC [edited], March 19):** During week 10 (March 7-13, 2010), influenza activity remained at approximately the same levels as last week in the U.S. 200 (5.6%) specimens tested by U.S. World Health Organization and National Respiratory and Enteric Virus Surveillance System collaborating laboratories and reported to CDC/Influenza Division were positive for influenza. All subtyped influenza A viruses reported to CDC were 2009 influenza A (H1N1) viruses. The proportion of deaths attributed to pneumonia and influenza (P&I) was below the epidemic threshold. Two influenza-associated pediatric deaths were reported. One death was associated with 2009 influenza A (H1N1) virus infection and one death was associated with an influenza A virus for which the subtype was undetermined. The proportion of outpatient visits for influenza-like illness (ILI) was 1.8%, which is below the national baseline of 2.3%. One of 10 regions (Region 4) reported ILI above its region-specific baseline level. No states reported widespread influenza activity. Three states reported regional influenza activity. Puerto Rico and eight states reported local influenza activity. The District of Columbia, Guam and 31 states reported sporadic influenza activity. Eight states reported no influenza activity, and the U.S. Virgin Islands did not report.

Since August 30, 2009, CDC has received 267 reports of influenza-associated pediatric deaths that occurred during the current influenza season (48 deaths in children less than 2 years old, 30 deaths in children 2-4 years old, 99 deaths in children 5-11 years old, and 90 deaths in children 12-17 years old). Two hundred eighteen (82%) of the 267 deaths were due to 2009 influenza A (H1N1) virus infections, 48 were associated with an influenza A virus for which the subtype is undetermined, and one was associated with an influenza B virus infection. A total of 278 deaths in children associated with 2009 influenza A (H1N1) virus infection have been reported to CDC.

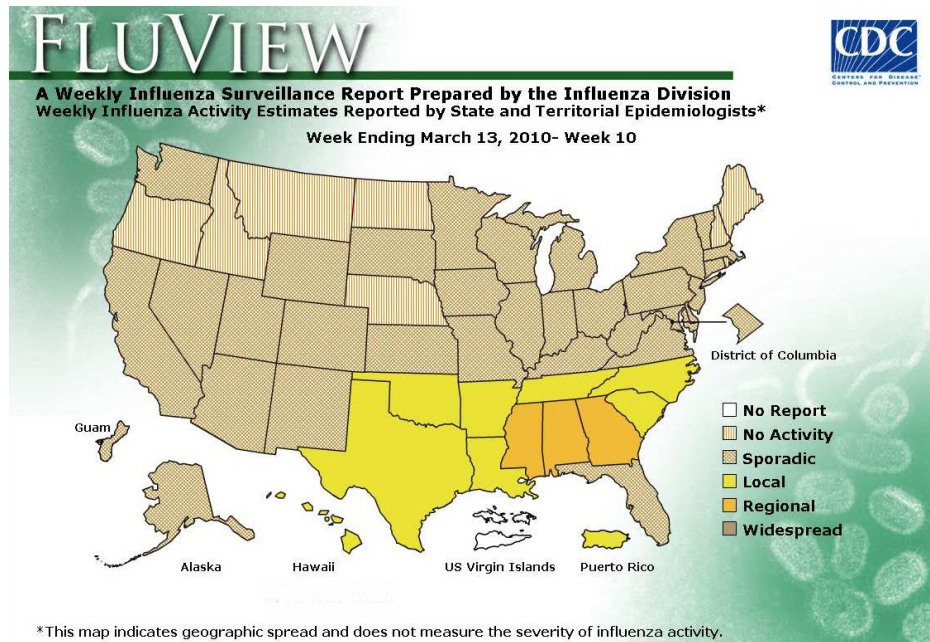
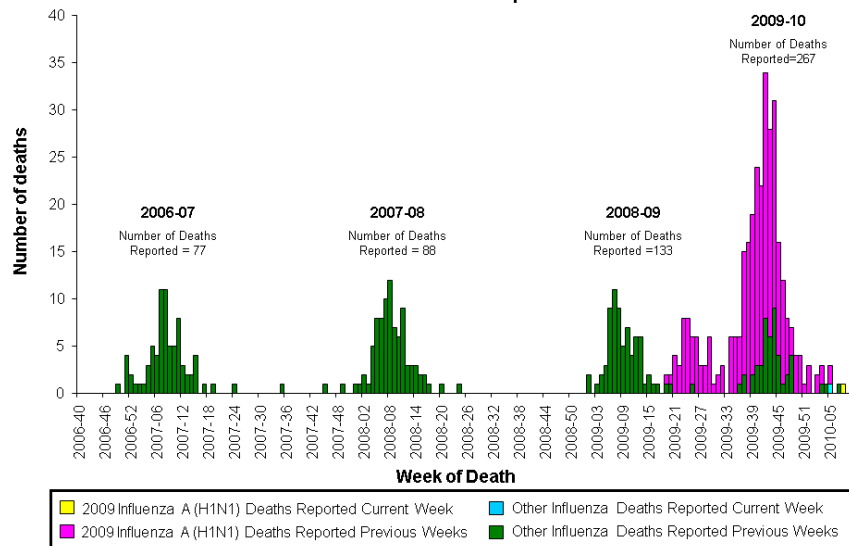
Among the 267 deaths in children, 141 children had specimens collected for bacterial culture from normally sterile sites and 49 (34.8%) of the 141 were positive; *Streptococcus pneumoniae* was identified in 11 (22.4%) of the 49 children and *Staphylococcus aureus* was identified in 14 (28.6%) of the 49 children. Four *S. aureus* isolates were sensitive to methicillin, nine were methicillin resistant, and one did not have sensitivity testing performed. Thirty-two (65.3%) of the 49 children with bacterial coinfections were five years of age or older, and 17 (34.7%) of the 49 children were 12 years of age or older.

Laboratory-Confirmed Influenza-Associated Pediatric Deaths by Date and Type/Subtype of Influenza

Date	2009 H1N1 Influenza	Influenza A-Subtype Unknown	Seasonal Influenza	Total
Number of Deaths REPORTED for Current Week – Week 10 (Week ending March 13, 2010)	1	1	0	2
Number of Deaths OCCURRED since August 30, 2009	218	48	1	267
Number of Deaths OCCURRED since April 26, 2009	278	51	2	331

To access the entire CDC weekly surveillance report, visit <http://www.cdc.gov/flu/weekly/fluactivity.htm>

## Number of Influenza-Associated Pediatric Deaths by Week of Death: 2006-07 season to present



From <http://www.cdc.gov/h1n1flu/updates/us/#totalcases>:

*U.S. Influenza and Pneumonia-Associated Hospitalizations and Deaths from Aug 30, 2009–Mar 13, 2010*

**Cases Defined by**  
Influenza Laboratory-Tests\*\*

**Hospitalizations**  
41,322

**Deaths**  
2,061

\*\*States report weekly to CDC either 1) laboratory-confirmed influenza hospitalizations and deaths or 2) pneumonia and influenza syndrome-based cases of hospitalization and death resulting from all types or subtypes of influenza. Although only the laboratory confirmed cases are included in this report, CDC continues to analyze data both from laboratory confirmed and syndromic hospitalizations and deaths.

**International (WHO, March 19): PANDEMIC (H1N1) 2009:** During weeks 7-8, pandemic influenza A (H1N1) 2009 virus activity continued to decrease in most countries and was not the predominant circulating virus reported in a number of countries in Asia and the Middle East. China, China Hong Kong Special Administrative Region, Iran (Islamic Republic of) and Mongolia all reported influenza B as the predominant virus.

Regional outbreaks of pandemic influenza A (H1N1) 2009 activity were reported in Armenia, Austria, China, Greece, Italy, Mongolia and Peru. Local levels of pandemic influenza A (H1N1) 2009 activity were reported in Argentina, Brazil, Cambodia, Ghana, Japan, Republic of Moldova, Russian Federation, Senegal and United States of America.



Sporadic pandemic influenza A (H1N1) 2009 activity was reported in Algeria, Australia, Austria, Belarus, Belgium, Bosnia and Herzegovina, Bulgaria, Cameroon, Canada, Chile, China Hong Kong Special Administrative Region, Croatia, Czech Republic, Denmark, Estonia, France, Germany, Georgia, Hungary, Indonesia, Iran (Islamic Republic of), Israel, Italy, Kenya, Kyrgyzstan, Latvia, Lithuania, Luxembourg, Madagascar, Malta, Mexico, Montenegro, Norway, Poland, Portugal, Republic of Korea, Romania, Rwanda, Serbia, South Africa, Spain, Sweden, Switzerland, Thailand, Uganda, Ukraine, United Kingdom and Zambia.

SEASONAL INFLUENZA: Influenza B activity was high in China, China Hong Kong Special Administrative Region, Iran (Islamic Republic of), Mongolia and increasing in the Russian Federation and Sweden. Influenza H1N1 and H3N2 was also detected at low levels in China. Sporadic seasonal influenza activity was observed in Algeria (H3), Angola (B), Australia (H3,B), Canada (B), China Hong Kong Special Administrative Region (H3,B), Cameroon (B), Ghana (H3), Iran (Islamic Republic of) (B), Japan (H3,B), Latvia (B), Kenya (B), Poland (B), Romania (B), Russian Federation (H1,H3,B), Senegal (H1), Spain (B), Sweden (B), Thailand (H3,B), Uganda (H3,B), Ukraine (B), United Kingdom (B), United Republic of Tanzania (H3,B), United States of America (H3,B) and Zambia (H1,B).

Armenia, Azerbaijan, Bolivia (Plurinational State of), Central African Republic, El Salvador, Ethiopia, France - New Caledonia, Mozambique, Netherlands, New Zealand, Panama, Slovakia, Slovenia, The former Yugoslav Republic of Macedonia, Tunisia and Uzbekistan reported no influenza activity.

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MDCH reported **SPORADIC INFLUENZA ACTIVITY** to the CDC for the week ending March 20, 2010.

For those interested in additional influenza vaccination and education information, the MDCH *FluBytes* is available at [http://www.michigan.gov/mdch/0,1607,7-132-2940\\_2955\\_22779\\_40563-125027--,00.html](http://www.michigan.gov/mdch/0,1607,7-132-2940_2955_22779_40563-125027--,00.html).

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### ***Novel Influenza Activity and Other News***

**WHO Pandemic Phase:** Phase 6 – characterized by increased and sustained transmission in the general population. Human to human transmission of an animal or human-animal influenza reassortant virus has caused sustained community level outbreaks in at least two WHO regions.

**National, Research (NIH press release, March 24):** Although they emerged more than 90 years apart, the influenza viruses responsible for the pandemics of 1918 and 2009 share a structural detail that makes both susceptible to neutralization by the same antibodies. Scientists led by Gary J. Nabel, M.D., Ph.D., of the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, describe the molecular basis for this shared vulnerability and suggest how it might be exploited to design vaccines matched to future pandemic influenza virus strains. The research appears online today in the journal *Science Translational Medicine*.

"This study defines an unexpected similarity between two pandemic-causing strains of influenza," says NIAID Director Anthony S. Fauci, M.D. "It gives us a new understanding of how pandemic viruses evolve into seasonal strains, and, importantly, provides direction for developing vaccines to slow or prevent that transformation."

In one set of experiments, the NIAID scientists and their colleagues including Terrence M. Tumpey, Ph.D., of the Centers for Disease Control and Prevention, injected mice with a vaccine made from inactivated 1918 influenza virus. Then they exposed the mice to high levels of 2009 H1N1 virus. All of the vaccinated mice survived. The reverse was also true: Mice vaccinated with inactivated 2009 H1N1 virus and then exposed to 1918 virus were protected from death. The researchers concluded that vaccination with either pandemic virus caused the mice to produce antibodies capable of neutralizing the other virus.

"This is a surprising result," notes Dr. Nabel. "We wouldn't have expected that cross-reactive antibodies would be generated against viruses separated by so many years."

Ordinarily, he explains, antibodies made in response to one year's seasonal flu strain do not fully react with, or cross-neutralize, seasonal flu strains that come along just a few years later. This is due in part to slight, yearly changes in the amino acid sequence of hemagglutinin (HA), a viral surface protein. The amino acid sequences of the 1918 and 2009 H1N1 influenza viruses in a portion of HA called the globular head differ by about 20 percent. That difference is on a par with amino acid divergence in the HA head region among seasonal strains, so the researchers reasoned that antibody cross-neutralization in the pandemic viruses must be due to some feature besides simply the degree of amino acid variation.

In a series of experiments and computer modeling studies, Dr. Nabel and his team determined that both pandemic viruses lack a cap of sugar (glycan) molecules at two specific spots on the top of HA's globular head. Without these sugars, both the 1918 and 2009 pandemic viruses have unfettered access to the receptors that HA uses to enter human cells. This viral advantage quickly diminishes as immunity provided by neutralizing antibodies arises in people who have been infected (and recovered) or when people are vaccinated.

In contrast to the 1918 and 2009 viruses, when the investigators analyzed the structure of seasonal flu strains that had circulated between 1977 and 2008, they found that 97.8 percent had one glycan molecule covering the HA's head, while 87.8 percent of the strains had two glycans. "The glycans act like an umbrella that shields the virus from the immune system," says Dr. Nabel. "They create a physical barrier over the virus and prevent antibody neutralization."

Further analysis of influenza sequences collected prior to 1977 revealed that the HA protein in the descendants of the 1918 influenza virus acquired glycans by the early 1940's. "Our study points to the key role played by glycans in protecting hemagglutinin from neutralization as pandemic viruses evolve into seasonal ones," says Dr. Nabel.

Next, the researchers engineered mutant pandemic flu viruses by placing sugar molecules on the two critical regions at the top of the globular head. Once covered, antibodies could no longer recognize and neutralize the virus. However, says Dr. Nabel, the sugar-capped viruses did perform well as vaccines.

In their last series of experiments, the investigators added sugar molecules to a 1918 influenza virus and vaccinated mice with it. The mice produced antibodies able to neutralize the original, sugar-free version of the 1918 virus. "We can use this knowledge to preemptively design vaccines with glycosylated versions of the newly emerged 2009 H1N1 pandemic influenza virus," says Dr. Nabel. Such a vaccine, he adds, would protect against the pandemic virus and might also limit the virus's chances of acquiring a sugar shield that would allow it to entrench itself as a seasonal variant.

REFERENCE: C-J Wei et al. Cross-neutralization of 1918 and 2009 influenza viruses: Role of glycans in viral evolution and vaccine design. *Science Translational Medicine*. DOI: 10.1126/scitranslmed.3000799 (2010).

**International, Research (Reuters Health, March 19):** In a study of Japanese schoolchildren, vitamin D supplements taken during the winter and early spring helped prevent seasonal flu and asthma attacks.

The idea for the study, study chief Dr. Mitsuyoshi Urashima, told Reuters Health, came from an earlier study looking at whether vitamin D could help prevent the bone-thinning disease osteoporosis. The researchers in that study noticed that people taking vitamin D were three times less likely to report cold and flu symptoms.

This led Urashima, of Jikei University School of Medicine, Tokyo, and colleagues to randomly assign a group of 6- to 15-year-old children to take vitamin D3 supplements (1,200 international units daily) or inactive placebo during a cold and flu season.

Vitamin D3, or cholecalciferol, is more readily absorbed by the body and more potent than vitamin D2, or ergocalciferol, the form often found in multivitamins.

During the study, conducted between December 2008 and March 2009, 31 of 167 children taking placebo caught influenza A, the most common form of the virus, compared with only 18 of 167 taking vitamin D.

The vitamin D group was 58 percent less likely to catch influenza A, the researchers report in the *American Journal of Clinical Nutrition*.

Vitamin D also appeared to suppress asthma attacks in children with a history of asthma. Two children taking vitamin D had asthma attacks during the study, compared to 12 children taking placebo. Urashima admitted to being a bit surprised by this finding and hopes to confirm it in a randomized trial targeting children with asthma.

Dr. Adit Ginde, of University of Colorado Denver School of Medicine, who was not involved in the study, told Reuters Health: "This is the first time a study has been done that rigorously shows that vitamin D supplementation can reduce a type of influenza in a dedicated clinical trial." Ginde and colleagues

published a study a year ago showing that asthmatics with lower vitamin D levels were at five times the risk for colds and flu.

In the Japanese study, vitamin D supplementation did not prevent influenza type B, which tends to appear later in the flu season than the "A" flu variety.

Ginde said there is no solid explanation for why vitamin D prevented influenza A and not influenza B. "The immune system fights different viruses in different ways. This finding needs to be explored in more detail," Ginde said.

Based on the current study, giving kids vitamin D supplements during the winter may help reduce cases of influenza A, the researchers conclude. Urashima suggests that children could take 1,200 IU per day starting in September to prevent flu and asthma attacks during the flu season, but best for parents to check with their pediatrician first.

**Michigan Wild Bird Surveillance (USDA, as of March 25):** For the 2009 testing season (April 1, 2009-March 31, 2010), HPAI subtype H5N1 has not been recovered from any of the 111 Michigan samples tested to date, including 58 live wild birds, 39 hunter-killed birds and 14 morbidity/mortality specimens. H5N1 HPAI has not been recovered from 19,104 samples tested nationwide. For more information, visit the National HPAI Early Detection Data System at <http://wildlifedisease.nbi.gov/ai/>.

To learn about avian influenza surveillance in Michigan wild birds or to report dead waterfowl, go to Michigan's Emerging Disease website at <http://www.michigan.gov/emergingdiseases>.

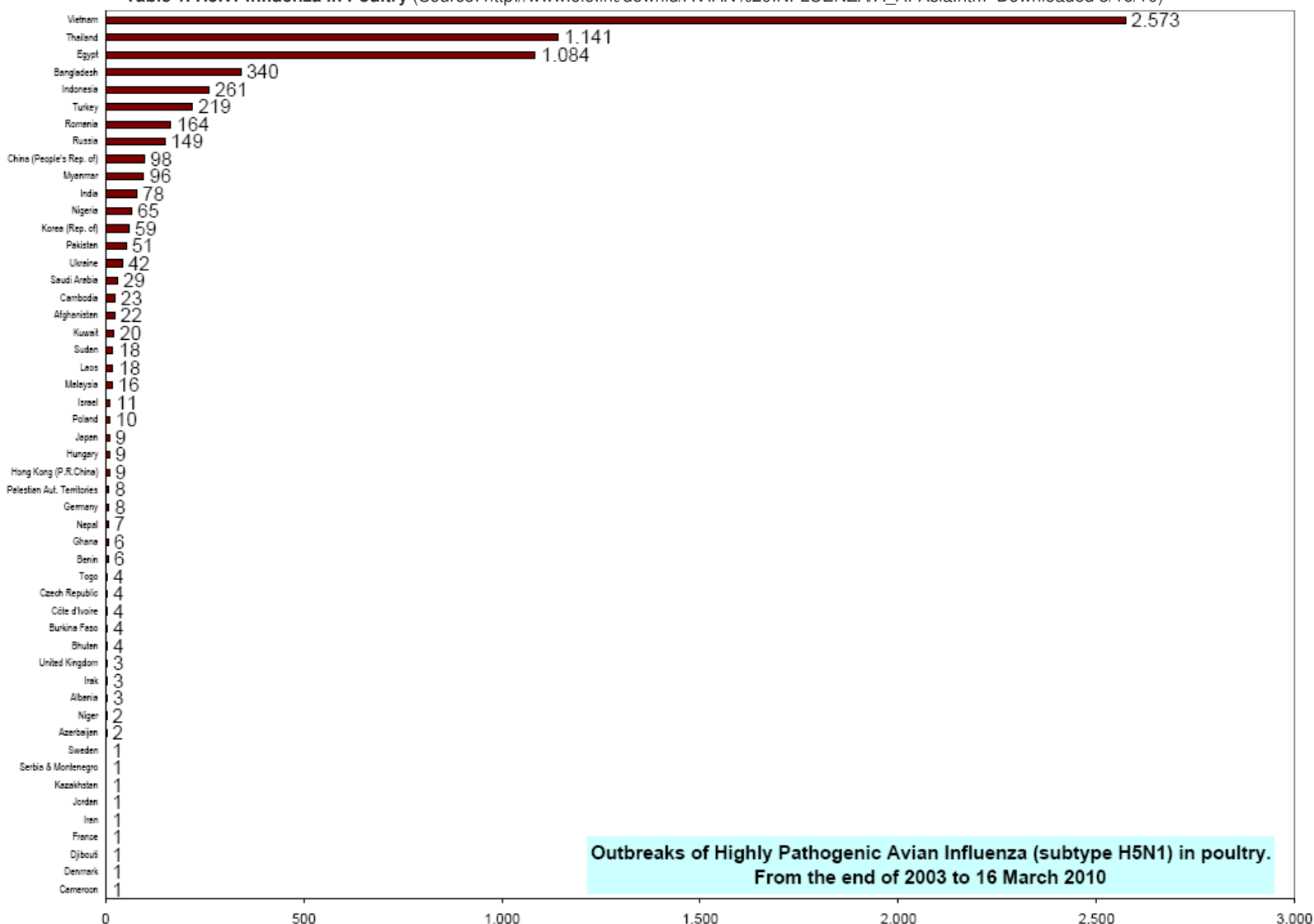
**Please contact Susan Peters at [PetersS1@Michigan.gov](mailto:PetersS1@Michigan.gov) with any questions regarding this newsletter or to be added to the weekly electronic mailing list.**

**Contributors**

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**MDCH Bureau of Laboratories – Anthony Muyombwe, PhD; Victoria Vavricka, MS**

**Table 1. H5N1 Influenza in Poultry** (Source: [http://www.oie.int/downld/AVIAN%20INFLUENZA/A\\_AI-Asia.htm](http://www.oie.int/downld/AVIAN%20INFLUENZA/A_AI-Asia.htm) Downloaded 3/16/10)



**Outbreaks of Highly Pathogenic Avian Influenza (subtype H5N1) in poultry.  
From the end of 2003 to 16 March 2010**

**Table 2. H5N1 Influenza in Humans - Cases up to March 16, 2010.** [http://www.who.int/csr/disease/avian\\_influenza/country/cases\\_table\\_2010\\_03\\_16/en/index.html](http://www.who.int/csr/disease/avian_influenza/country/cases_table_2010_03_16/en/index.html). Downloaded 3/17/2010. Cumulative number of lab-confirmed cases reported to WHO. Total cases includes deaths.

Country	2003		2004		2005		2006		2007		2008		2009		2010		Total	
	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths
Azerbaijan	0	0	0	0	0	0	8	5	0	0	0	0	0	0	0	0	8	5
Bangladesh	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0
Cambodia	0	0	0	0	4	4	2	2	1	1	1	0	1	0	0	0	9	7
China	1	1	0	0	8	5	13	8	5	3	4	4	7	4	0	0	38	25
Djibouti	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0
Egypt	0	0	0	0	0	0	18	10	25	9	8	4	39	4	16	5	106	32
Indonesia	0	0	0	0	20	13	55	45	42	37	24	20	21	19	1	1	163	135
Iraq	0	0	0	0	0	0	3	2	0	0	0	0	0	0	0	0	3	2
Lao People's Democratic Republic	0	0	0	0	0	0	0	0	2	2	0	0	0	0	0	0	2	2
Myanmar	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0
Nigeria	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	1	1
Pakistan	0	0	0	0	0	0	0	0	3	1	0	0	0	0	0	0	3	1
Thailand	0	0	17	12	5	2	3	3	0	0	0	0	0	0	0	0	25	17
Turkey	0	0	0	0	0	0	12	4	0	0	0	0	0	0	0	0	12	4
Viet Nam	3	3	29	20	61	19	0	0	8	5	6	5	5	5	4	1	116	58
Total	4	4	46	32	98	43	115	79	88	59	44	33	73	32	21	7	489	289